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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 4	DEC 18	CA/CAplus patent kind codes updated
NEWS 5	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 7	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 9	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 12	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 13	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 14	JAN 29	PHAR reloaded with new search and display fields
NEWS 15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 19	FEB 26	MEDLINE reloaded with enhancements
NEWS 20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 25	MAR 16	CASREACT coverage extended
NEWS 26	MAR 20	MARPAT now updated daily

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:28:11 ON 20 MAR 2007

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 18:28:29 ON 20 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 19 MAR 2007 HIGHEST RN 927525-36-8
DICTIONARY FILE UPDATES: 19 MAR 2007 HIGHEST RN 927525-36-8

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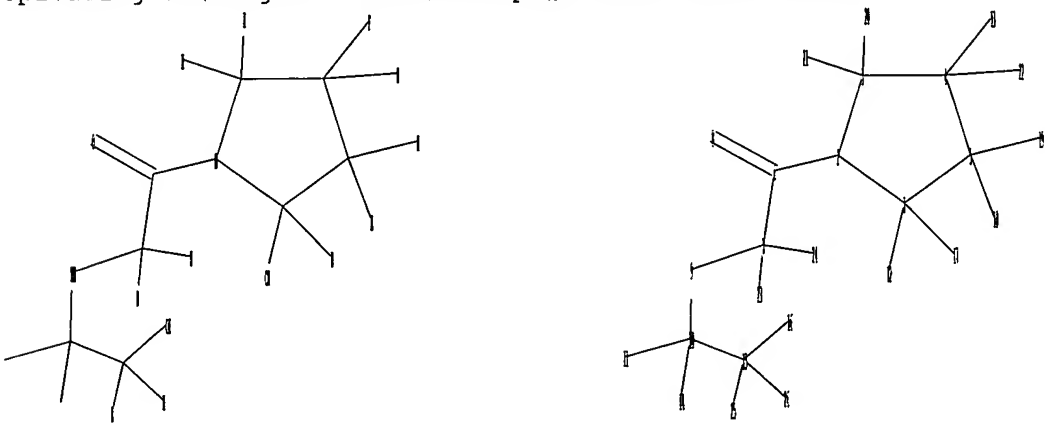
http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10525748.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
ring nodes :
1 2 3 4 5
chain bonds :
1-12 1-17 2-6 3-20 3-21 4-13 4-22 5-18 5-19 6-7 6-8 7-9 7-23 7-24
9-10 10-11 10-14 10-15 15-16 15-25 15-26
ring bonds :
1-2 1-5 2-3 3-4 4-5

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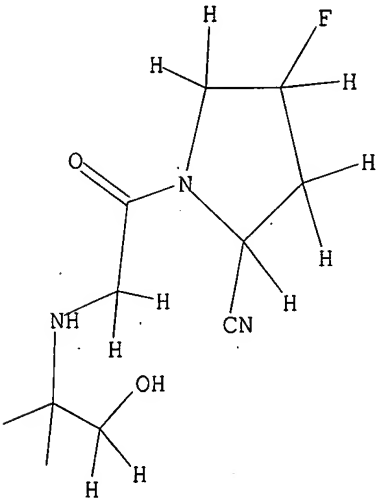
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 4-5 6-8 7-9 9-10 15-16
exact bonds :
1-12 1-17 3-20 3-21 4-13 4-22 5-18 5-19 6-7 7-23 7-24 10-11 10-14
10-15 15-25 15-26

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS
26:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 18:28:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 27 TO ITERATE

100.0% PROCESSED 27 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 229 TO 851
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 18:28:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 476 TO ITERATE

10525748

100.0% PROCESSED 476 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L3 6 SEA SSS FUL L1

=> fil hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'HCAPLUS' ENTERED AT 18:29:05 ON 20 MAR 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Mar 2007 VOL 146 ISS 13
FILE LAST UPDATED: 19 Mar 2007 (20070319/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 11 L3

=> s l4 and benzenesulfonate
6733 BENZENESULFONATE
L5 3 L4 AND BENZENESULFONATE

=> d ibib abs ed hitstr 1-3

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1073986 HCAPLUS
DOCUMENT NUMBER: 143:353363
TITLE: Dipeptidylpeptidase IV inhibitors containing cyanopyrrolidine derivatives
INVENTOR(S): Fukushima, Hiroshi; Hiradate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005272457	A	20051006	JP 2005-49585	20050224
PRIORITY APPLN. INFO.:			JP 2004-49774 A	20040225

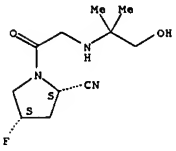
AB The invention relates to a dipeptidylpeptidase IV (DPPIV) inhibitor characterized by containing (2S,4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine benzenesulfonate (I) or its hydrate as an active component, wherein I shows improved storage stability, and suitable for use for treatment of diabetes and immune disease.
ED Entered STN: 07 Oct 2005
IT 667865-69-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dipeptidylpeptidase IV inhibitors containing (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine benzenesulfonate)
RN 667865-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 625110-37-4
CMF C11 H18 F N3 O2

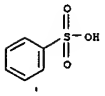
Absolute stereochemistry.

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



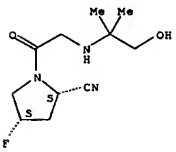
CM 2

CRN 98-11-3
CMF C6 H6 O3 S

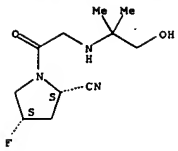


IT 625110-37-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dipeptidylpeptidase IV inhibitors containing (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine benzenesulfonate)
RN 625110-37-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

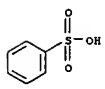


L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 98-11-3
CMF C6 H6 O3 S



IT 865853-31-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidylpeptidase IV inhibitors containing (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine benzenesulfonate or its hydrate)
RN 865853-31-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt), hydrate (9CI) (CA INDEX NAME)

CM 1

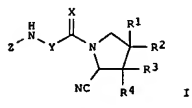
CRN 625110-37-4
CMF C11 H18 F N3 O2

Absolute stereochemistry.

L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:70491 HCAPLUS
DOCUMENT NUMBER: 142:127593
TITLE: Therapeutic agents for chronic renal disorders containing dipeptidyl peptidase IV inhibitors, especially cyanopyrrolidine derivatives
INVENTOR(S): Okuyama, Shigeru; Miyata, Noriyuki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005023038	A	20050127	JP 2003-191787	20030704
PRIORITY APPLN. INFO.:			JP 2003-191787	20030704

OTHER SOURCE(S): MARPAT 142:127593
GI



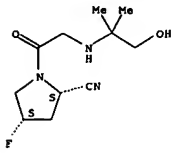
I

AB The therapeutic agents are claimed. The derivs. are I [R1-R4 = H, halo, OH, C1-5 alkoxy, C1-5 alkyl; R1 and R2, R3 and R4 may be bonded together to form :O, NHOH, C1-5 alkoxyimino, C1-5 alkylidene; X = O, S; Y = CR5R6 [R5-R6 = H, halo, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl], CR7R8CR9R10 [R7-R10 = H, halo, (un)substituted C1-10 alkyl; R7 and R9 may be bonded together to form an (un)substituted C3-8 cycloalkyl, C4-8 cycloalkenyl, C5-10 bicycloalkenyl]; Z = H, (un)substituted C1-10 alkyl; Y and Z may be bonded to form a (un)substituted c2-20 cyclic amino group] or their pharmacol. acceptable salts. Thus, IC50 of (2S,4S)-2-Cyano-fluoro-1-[[2-hydroxy-1,1-dimethyl]ethylamino]acetylpyrrolidine benzenesulfonate (II) against human peripheral blood-derived I was 5.4 nM. II also decreased urinary protein and albumin excretions in ZSF-1 spontaneously diabetic rats.
ED Entered STN: 27 Jan 2005
IT 667865-69-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for chronic renal disorders containing dipeptidyl
o especially cyanopyrrolidine derivs.)
RN 667865-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt) (9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CM 1

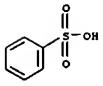
CRN 625110-37-4
CMF C11 H18 F N3 O2

Absolute stereochemistry.



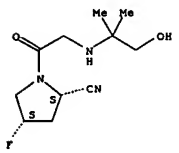
CM 2

CRN 98-11-3
CMF C6 H6 O3 S



L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
silica gel chromatog., 0.22 g (2S,4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethylethyl)amino]acetylpyrrolidine (II). II (20 g) was dissolved in 300 mL ethanol with warming, treated with a soln. of 15.2 g benzenesulfonic acid monohydrate in 30 mL methanol, upon which a powder pptd. To the suspension obtained was added 330 mL Et2O followed by filtration to give I as a colorless powder. I 10, cryst. cellulose 68, and magnesium stearate 2 mg were mixed by a MIX-ROTOR VMR-5 for 1 h and stored at 65° for 1 wk. The residual ratio of I was 99.1% vs. 91.6% for II methanesulfonate.
ED Entered STN: 14 Mar 2004
IT 426844-00-0P, (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethylethyl)amino]acetylpyrrolidine hydrochloride 667865-68-1P 667865-69-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (2S,4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethylethyl)amino]acetylpyrrolidine benzenesulfonate as dipeptidyl peptidase inhibitor)
RN 426844-00-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 667865-68-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 625110-37-4
CMF C11 H18 F N3 O2

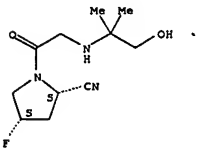
Absolute stereochemistry.

L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203807 HCAPLUS
DOCUMENT NUMBER: 140:235600
TITLE: Preparation of benzenesulfonate of 4-fluoro-2-cyanopyrrolidine derivative
INVENTOR(S): Fukushima, Hiroshi; Hiratate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co.,ltd., Japan
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004020407	A1	20040311	WO 2003-JP10828		20030827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2496623	A1	20040311	CA 2003-2496623		20030827
AU 2003261748	A1	20040319	AU 2003-261748		20030827
EP 1535907	A1	20050601	EP 2003-791325		20030827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013831	A	20050705	BR 2003-13831		20030827
CN 1678575	A	20051005	CN 2003-820336		20030827
JP 3746063	B2	20060215	JP 2004-532725		20030827
NZ 538956	A	20060831	NZ 2003-538956		20030827
NO 2005000867	A	20050218	NO 2005-867		20050218
US 2006106087	A1	20060518	US 2005-525748		20051011
PRIORITY APPLN. INFO.:			JP 2002-249821	A	20020829
			WO 2003-JP10828	W	20030827

OTHER SOURCE(S): CASREACT 140:235600
AB Disclosed is (2S,4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine benzenesulfonate (I) which shows an excellent dipeptidyl peptidase IV (DPPIV) inhibitory activity and has properties required as a medicine, for example, a high stability. This compound can be easily obtained in the form of highly stable crystals having a uniform shape and has a high solid stability. Thus, 0.71 g (2S,4S)-1-bromoacetyl-2-cyano-4-fluoropyrrolidine was added to a solution of 0.54 g 2-amino-2-methyl-1-propanol in 7.5 mL THF and 2.5 mL ethanol under ice-cooing, stirred at room temperature for 1 h, and filtered to give, after

L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

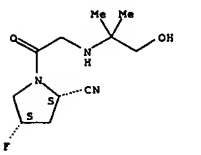
CRN 75-75-2
CMF C H4 O3 S

RN 667865-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 625110-37-4
CMF C11 H18 F N3 O2

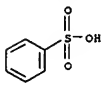
Absolute stereochemistry.



CM 2

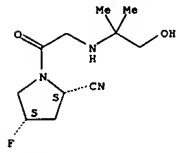
CRN 98-11-3
CMF C6 H6 O3 S

L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 625110-37-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (2S,4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethylethyl)amino]acetylpyrrolidine benzenesulfonate as dipeptidyl peptidase inhibitor)
RN 625110-37-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

10525748

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     FILE 'REGISTRY' ENTERED AT 18:28:29 ON 20 MAR 2007
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            6 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 18:29:05 ON 20 MAR 2007
L4           11 S L3
L5            3 S L4 AND BENZENESULFONATE

=> s l4 not l5
L6            8 L4 NOT L5

=> d ed ibib abs hitstr 1-8
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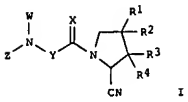
L6 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 04 Aug 2006
ACCESSION NUMBER: 2006:769218 HCAPLUS
DOCUMENT NUMBER: 145:217912
TITLE: Cyanopyrrolidine derivative-containing composition for
solid pharmaceutical preparations, and process for producing the same
INVENTOR(S): Yazaki, Hiroaki; Ikuta, Hiroshi
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006080412	A2	20060803	WO 2006-JP301258	20060120
WO 2006080412	A3	20060921		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-22193 A 20050128

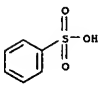
OTHER SOURCE(S): MARPAT 145:217912
GI



I

AB The present invention relates to a composition for solid pharmaceutical prepns.
consisting of a cyanopyrrolidine derivative, to a solid pharmaceutical preparation
containing the composition, and to a process for producing the solid pharmaceutical

L6 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

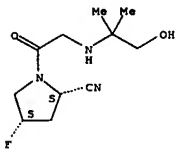


L6 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
prepn. The compn. essentially consisting of a cyanopyrrolidine deriv. represented by the following general formula (I) or a pharmaceutically acceptable salt thereof, and at least one stabilizing ingredient selected from the group consisting of sugars and sugar alcs. Specifically, for the
formula of the present invention, R1 represents a halogen atom or a hydroxyl group, R3 and R4 may be the same or different, each represents, for example, a hydrogen atom or a halogen atom, X represents an oxygen atom or a sulfur atom, Y represents, for example, a group represented by -CR5R6- (wherein R5 and R6 may be the same or different, each represents, for example, a hydrogen atom or a halogen atom), W represents, for example, a hydrogen atom or an acyl group derived from naturally occurring
amino acids, and Z represents, for example, a hydrogen atom or an alkyl group of 1 to 10 carbon atoms which may be substituted with one or more substituents selected from the group consisting of a halogen atom, a hydroxyl group, a hydroxylalkyl group of 1 to 5 carbon atoms, a carboxyl group, a mercapto group and the like.
IT 667865-69-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyanopyrrolidine derivative-containing composition for solid pharmaceutical
preprns., and process for producing the same)
RN 667865-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 625110-37-4
CMF C11 H18 F N3 O2

Absolute stereochemistry.



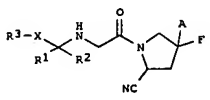
CM 2

CRN 98-11-3
CMF C6 H6 O3 S

L6 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 22 Jun 2006
ACCESSION NUMBER: 2006:598046 HCAPLUS
DOCUMENT NUMBER: 145:76699
TITLE: Medicines containing cyanofluoropyrrolidine derivatives as dipeptidylpeptidase IV inhibitors
INVENTOR(S): Fukushima, Hiroshi; Takahashi, Masato; Mikami, Ayako
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 62 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006160733	A	20060622	JP 2005-328431	20051114
PRIORITY APPLN. INFO.:			JP 2004-329901 A	20041115

OTHER SOURCE(S): MARPAT 145:76699
GI

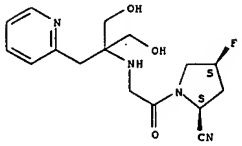


I

AB The invention relates to medicines containing cyanofluoropyrrolidine derivs. I
(A = H, F; R1, R2 = H, C1-6 alkyl, C3-6 cycloalkyl, C2-6 alkenyl, etc.; X = single bond, C1-3 alkylene; R3 = substituted amide, substituted sulfonyl, heteroaryl, etc.), or its salt or hydrates as active components.
The medicines have dipeptidylpeptidase IV (DPPIV) inhibitory effects, and suitable for use for treatment and/or prevention of diabetes and immune disease. For example, (2S,4S)-2-cyano-4-fluoro-1-[[2-(3,4-methylenedioxybenzoyl)amino-1,1-dimethyl]ethylamino]acetylpyrrolidine was prepared, and examined for its effect on DPPIV activity in vitro.
IT 798572-23-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicines containing cyanofluoropyrrolidine derivs. as dipeptidylpeptidase
IV inhibitors)
RN 798572-23-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-bis(hydroxymethyl)-2-(2-pyridinyl)ethyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

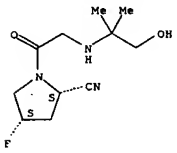
Absolute stereochemistry.

L6 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L6 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Reactant or reagent)
(prepn. of cyanofluoropyrrolidine derivs. as dipeptidyl peptidase IV inhibitors for treatment of diabetes, immune diseases, etc.)
RN 426844-00-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

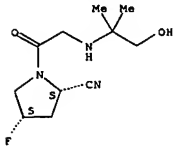
Absolute stereochemistry.



● HCl

RN 625110-37-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

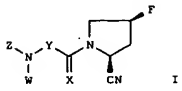
Absolute stereochemistry.



L6 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 02 Jun 2005
ACCESSION NUMBER: 2005:470090 HCAPLUS
DOCUMENT NUMBER: 143:7593
TITLE: Pharmaceuticals containing cyanopyrrolidine derivatives as dipeptidyl peptidase IV inhibitors
INVENTOR(S): Fukushima, Hiroshi; Hiradate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005139107	A	20050602	JP 2003-375835	20031105
PRIORITY APPLN. INFO.:			JP 2003-375835	20031105

OTHER SOURCE(S): MARPAT 143:7593
GI



AB Pharmaceuticals, useful for treatment of diseases, e.g. diabetes, immune diseases, etc., contain cyanopyrrolidine derivs. I [W = acyl derived from amino acids, CO2CHW2OW1 (W1 = C1-5 alkanoyl, arylcarbonyl, C1-5 alkyl; W2 = H, C1-5 alkyl), CW4:CHCOW3 (W3, W4 = H, C1-5 alkyl); X = O, S; Y = CR5R6 (R5, R6 = H, halo, C1-10 alkyl optionally substituted with halo, guanidyl, imidazolyl, indolyl, etc., C2-10 alkenyl optionally substituted with halo, OH, amino, etc.), CR7R8CR9R10 [R7-R10 = H, halo, C1-10 alkyl optionally substituted, or CR7R8 may be (un)substituted C3-8 cycloalkyl, C4-8 cycloalkenyl, C5-10 dicycloalkyl, C5-10 bicycloalkenyl]; Z = H, C1-10 alkyl optionally substituted with halo, OH, C1-5 alkylthio, pyridyl, etc.; Z may be bonded to Y to form C2-10 cyclic amino optionally substituted with halo, OH, amino, etc.] and their pharmacol. acceptable salts. Thus, (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine hydrochloride (preparation given) inhibited human dipeptidyl peptidase IV at IC50 0.6 nM.
IT 426844-00-0P, (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine hydrochloride 625110-37-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

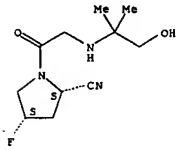
L6 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 24 Feb 2005
ACCESSION NUMBER: 2005:158636 HCAPLUS
DOCUMENT NUMBER: 142:261782
TITLE: Process for preparation of cis-4-fluoro-L-proline derivatives
INVENTOR(S): Tomisawa, Kazuyuki; Tatsuta, Dai; Yoshida, Tomomichi; Yokoo, Chihiro
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016880	A1	20050224	WO 2004-JP11827	20040818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004265182	A1	20050224	AU 2004-265182	20040818
CA 2534884	A1	20050224	CA 2004-2534884	20040818
EP 1657237	A1	20060517	EP 2004-771788	20040818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1839120	A	20060927	CN 2004-80023726	20040818
NO 2006000703	A	20060313	NO 2006-703	20060214
US 2006281927	A1	20061214	US 2006-568708	20060804
PRIORITY APPLN. INFO.:			JP 2003-207718 A	20030818
			WO 2004-JP11827 W	20040818

OTHER SOURCE(S): CASREACT 142:261782; MARPAT 142:261782
AB This invention pertains to a method for producing high purity cis-4-fluoro-L-proline derivs., which comprises reacting a trans-4-hydroxy-L-proline derivative with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in the presence of a HF scavenger. For example, (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid Me ester was reacted with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in CH2Cl2 in the presence of NaF to give (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid Me ester. This invention provides a convenient method to prepare cis-4-fluoro-L-proline derivs. in high yield under mild conditions at low cost.
IT 625110-37-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of cis-4-fluoro-L-proline derivs. via fluorination)
RN 625110-37-4 HCAPLUS

L6 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

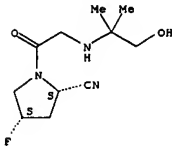


IT 667865-69-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of cis-4-fluoro-L-proline derivs. via fluorination)
RN 667865-69-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, (2S,4S)-, monobenzenesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 625110-37-4
CMF C11 H18 F N3 O2

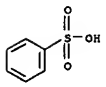
Absolute stereochemistry.



CM 2

CRN 98-11-3
CMF C6 H6 O3 S

L6 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



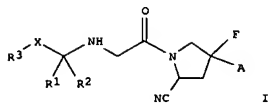
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 25 Nov 2004
ACCESSION NUMBER: 2004:1016009 HCAPLUS
DOCUMENT NUMBER: 142:6413
TITLE: Preparation of cyanofluoropyrrolidine derivatives as dipeptidylpeptidase IV inhibitors
INVENTOR(S): Fukushima, Hiroshi; Takahashi, Masato; Mikami, Ayako
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004101514	A1	20041125	WO 2004-JP6983	20040517
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004238719	A1	20041125	AU 2004-238719	20040517
CA 2525442	A1	20041125	CA 2004-2525442	20040517
EP 1627870	A1	20060222	EP 2004-733467	20040517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1791575	A	20060621	CN 2004-80013353	20040517
US 2006293297	A1	20061228	US 2005-556896	20051115
NO 2005005971	A	20051215	NO 2005-5971	20051215
PRIORITY APPLN. INFO.:			JP 2003-137062 A	20030515
			WO 2004-JP6983 W	20040517

OTHER SOURCE(S): MARPAT 142:6413
GI

L6 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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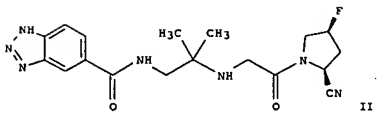
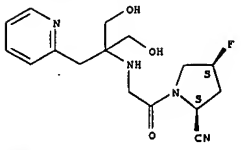


II

AB Title compds. I [A = H, F; R1, R2 = H, (un)substituted alkyl, etc.; further details on R1, R2 are given; X = single bond, alkylene; R3 = NR4COR5, etc.; R4, R5 = H, (un)substituted alkyl, etc.] were prepared For example, acylation of (2S,4S)-1-[(2-amino-1,1-dimethyl)ethylamino]acetyl-2-cyano-4-fluoropyrrolidine·2HCl with 1H-1,2,3-benzotriazole-5-carboxylic acid using N,N'-carbonyldiimidazole afforded compound II. In DPP IV (dipeptidylpeptidase IV) inhibition assays, compound II exhibited the IC50 value of 1.5 nM. Compds. I are claimed useful as dipeptidylpeptidase IV inhibitors for the treatment of diabetes, immunol. diseases.
IT 798572-23-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyanofluoropyrrolidine derivs. as dipeptidylpeptidase IV inhibitors for treatment of diabetes, immunol. diseases)
RN 798572-23-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-bis(hydroxymethyl)-2-(2-pyridinyl)ethyl]amino]acetyl]-4-fluoro-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

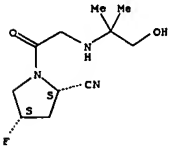


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 426844-00-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

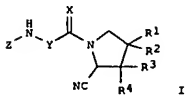


● HCl

L6 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 30 Jan 2004
ACCESSION NUMBER: 2004:76522 HCAPLUS
DOCUMENT NUMBER: 140:122807
TITLE: Dipeptidyl peptidase IV (DPPIV) inhibitors containing cyanopyrrolidines and their use as antidiabetic agents
INVENTOR(S): Fukushima, Hiroshi; Hiradate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 54 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004026820	A	20040129	JP 2003-130830	20030508
PRIORITY APPLN. INFO.:			JP 2002-134420 A	20020509

OTHER SOURCE(S): MARPAT 140:122807
GI

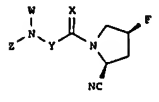


AB Title inhibitors contain cyanopyrrolidines I [R1 = halo, OH, C1-5 alkoxy, C1-5 alkyl; R2-R4 = H, halo, OH, C1-5 alkoxy, C1-5 alkyl; R1R2 and/or R3R4 may be O, hydroxyimino, C1-5 alkoxyimino, C1-5 alkylidene; X = O, S; Y = CR5R6, CR7R8CR9R10; R5-R10 = H, halo, (un)substituted C1-10 alkyl, etc.; Z = H, halo, OH, C1-5 hydroxyalkyl, SH, (un)substituted Ph, imidazolyl, indolyl, etc.] or their pharmacol. acceptable salts. Thus, (2S,4S)-2-aminocarbonyl-4-fluoropyrrolidine HCl salt was amidated with (2S,3S)-2-fluorenylmethoxycarbonylamino-3-methylpentanoic acid, treated with trifluoroacetic anhydride, deprotected, and converted into HCl salt to give (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine HCl salt, which inhibited DPPIV with IC50 value of 0.6 nM.
IT 426844-00-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyanopyrrolidines as dipeptidyl peptidase IV inhibitors for treatment of diabetes)

L6 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 21 Nov 2003
ACCESSION NUMBER: 2003:913142 HCAPLUS
DOCUMENT NUMBER: 139:381747
TITLE: Preparation of N-(aminoacyl)cyanofluoropyrrolidine derivatives as dipeptidyl peptidase IV inhibitors
INVENTOR(S): Fukushima, Hiroshi; Hiratate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095425	A1	20031120	WO 2003-JP5813	20030509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003235913	A1	20031111	AU 2003-235913	20030509
PRIORITY APPLN. INFO.:			JP 2002-134421 A	20020509
			WO 2003-JP5813 W	20030509

OTHER SOURCE(S): MARPAT 139:381747
GI



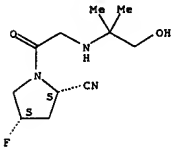
AB Cyanopyrrolidine derivs. represented by the general formula (I) or pharmaceutically acceptable salts thereof [wherein W is an acyl group derived from a natural amino acid, a group represented by the general formula W1-O-CH(W2)-O2C (wherein W1 is C1-5 alkanoyl, optionally substituted arylcarbonyl, or C1-5 alkyl; and W2 is hydrogen or C1-5 alkyl), or a group represented by the general formula W3COCH:C(W4) (wherein W3 and W4 are each hydrogen or C1-5 alkyl); X is oxygen or sulfur; Y is -CR5R6- (wherein R5 and R6 are each independently hydrogen, halogeno, or the like) or -CR7R8-CR9R10- (wherein R7, R8, R9, and R10 are each independently hydrogen, halogeno, or the like); and Z is hydrogen or optionally substituted C1-10 alkyl, or Y and Z together with the nitrogen

L6 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
atom adjacent to them may form an optionally substituted cyclic amino group having 2 to 10 carbon atoms] are prepd. These compds. are useful for the prevention or treatment of diseases or conditions which can be improved by inhibiting dipeptidyl peptidase IV (DPPIV), in particular diabetes and immune diseases. Thus, (2S,4S)-2-aminocarbonyl-4-fluoropyrrolidine hydrochloride was condensed with (2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoic acid using 1-hydroxybenzotriazole monohydrate and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of diisopropylamine in DMF at room temp. overnight to give (2S,4S)-2-aminocarbonyl-1-[(2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoyl]-4-fluoropyrrolidine which was treated with trifluoroacetic anhydride in THF under ice-cooling for 1.5 h followed by treatment with diethylamine in 1,2-dichloroethane under ice-cooling for
30
min and at room temp. for 5 h to give (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine (II). II was further converted into (2S,4S)-1-[(2S,3S)-2-[(1-acetoxyethoxycarbonyl)amino]-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine in two steps. II.HCl showed IC50 of 0.6 nM against DPPIV.

IT 426844-00-0P, (2S,4S)-2-Cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethylethyl)amino]acetylpyrrolidine hydrochloride 625110-37-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(aminoacyl)cyanofluoropyrrolidine derivs. as dipeptidyl
peptidase IV inhibitors for prevention or treatment of diabetes and immune diseases)

RN 426844-00-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

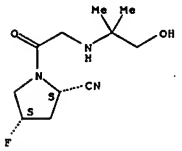


● HCl

RN 625110-37-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-

L6 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
dimethylethyl)amino]acetyl]-, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 18 May 2002
ACCESSION NUMBER: 2002:368450 HCAPLUS
DOCUMENT NUMBER: 136:386016
TITLE: Preparation of 2-cyanopyrrolidine derivatives as dipeptidyl peptidase IV (DPPIV) inhibitors
INVENTOR(S): Fukushima, Hiroshi; Hiratate, Akira; Takahashi, Masato; Kameo, Kazuya
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038541	A1	20020516	WO 2001-JP9818	20011109
WO 2002038541	A9	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
TW 243162	B	20051111	TW 2001-90127787	20011108
CA 2428271	A1	20020516	CA 2001-2428271	20011109
CA 2428271	C	20051227		
CA 2512476	A1	20020516	CA 2001-2512476	20011109
AU 200212745	A	20020521	AU 2002-12745	20011109
EE 200300175	A	20030616	EE 2003-175	20011109
EP 1333025	A1	20030806	EP 2001-981047	20011109
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BR 2001014851	A	20030916	BR 2001-14851	20011109
HU 200302248	A2	20031028	HU 2003-2248	20011109
CN 1474809	A	20040211	CN 2001-818732	20011109
NZ 525705	A	20040430	NZ 2001-525705	20011109
CN 1715269	A	20060104	CN 2005-10083201	20011109
CN 1772733	A	20060517	CN 2005-10125155	20011109
EP 1746086	A1	20070124	EP 2006-23245	20011109
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ZA 2003002591	A	20040702	ZA 2003-2591	20030402
NO 2003001949	A	20030708	NO 2003-1949	20030429
IN 2003CN00679	A	20050415	IN 2003-CN679	20030506
BG 107799	A	20040831	BG 2003-107799	20030510
US 2004072892	A1	20040415	US 2003-416370	20031103
NO 2005004429	A	20030708	NO 2005-4429	20050923
AU 2006246479	A1	20061221	AU 2006-246479	20061130
AU 2006246487	A1	20061221	AU 2006-246487	20061130

PRIORITY APPLN. INFO.:

JP 2000-344036	A	20001110
JP 2001-215766	A	20010716
AU 2002-12745	A3	20011109

L6 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CA 2001-2428271	A3	20011109
CN 2001-818732	A3	20011109
EP 2001-981047	A3	20011109
WO 2001-JP9818	W	20011109

OTHER SOURCE(S): MARPAT 136:386016
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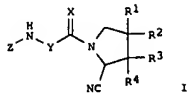


I

AB Cyanopyrrolidine derivs. represented by the general formula (I) or pharmaceutically acceptable salts thereof [wherein R1 is halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or, and R2 is hydrogen, halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or alternatively R1 and R2 are united
to form oxo, hydroxyimino, C1-5 alkoxyimino, or C1-5 alkylidene; R3 and R4
are each hydrogen, halogeno, hydroxyl, C1-5 alkoxy, or C1-5 alkyl or alternatively R3 and R4 are united to form oxo, hydroxyimino, C1-5 alkoxyimino, or C1-5 alkylidene; X is oxygen or sulfur; Y is CR5R6 (wherein R5 and R6 are each independently hydrogen, halogeno, or the like)
or CR7R8CR9R10 (wherein R7, R8, R9, and R10 are each independently hydrogen, halogeno, or the like, or alternatively R7 and R9 together with the carbon atoms adjacent thereto form C3-8 cycloalkyl or the like); and Z
is hydrogen or optionally substituted C1-10 alkyl, or alternatively Y and Z together with the nitrogen atom adjacent thereto form optionally substituted cyclic C2-10 amino] are prepared These compds. are useful for
the prevention or treatment of diabetes and immune diseases. Thus, N-acylation of (2S,4S)-2-(aminocarbonyl]-4-fluoropyrrolidine hydrochloride
using 1-hydroxybenzotriazole with (2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoic acid with and 1-ethyl-3-(3-dimethylaminopropyl]carbodiimide hydrochloride in the
presence of diisopropylethylamine in DMF/THF at room temperature overnight gave

(2S,4S)-2-(aminocarbonyl)-1-[(2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoyl]-4-fluoropyrrolidine which was treated with trifluoroacetic anhydride in THF under ice-cooling for 1.5 h to give (2S,4S)-2-cyano-1-[(2S,3S)-2-(9-fluorenylmethoxycarbonylamino)-3-methylpentanoyl]-4-fluoropyrrolidine (II). N-deprotection of II by
treatment with diethylamine in 1,2-dichloroethane under ice-cooling for
30
min and at room temperature for 5 h followed by treatment with 4 M HCl/dioxane

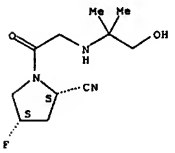
L6 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN (Continued)
and purifn. on silica gel column gave (2S,4S)-1-[(2S,3S)-2-amino-3-methylpentanoyl]-2-cyano-4-fluoropyrrolidine hydrochloride (III). III showed IC50 of 0.6 nM against DPPIV.

IT 426844-00-0P, (2S,4S)-2-Cyano-4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]pyrrolidine hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-cyanopyrrolidine derivs. as dipeptidyl peptidase IV inhibitors for prevention or treatment of diabetes and immune diseases)

RN 426844-00-0 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(2-hydroxy-1,1-dimethylethyl)amino]acetyl]-, monohydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	65.77	238.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.58	-8.58

STN INTERNATIONAL LOGOFF AT 18:30:46 ON 20 MAR 2007